

U.S. Patent Application Serial No. 10/630384
Amendment and Response to Office Action
Page 2 of 26

Amendment Of The Claims

Please amend the claims as follows. This listing of claims will replace all prior versions and listings of claims in the application.

Claims 1-15 (canceled)

Claim 16. (Currently amended) A method for detecting one or more biological entities in a sample, comprising:

(a) combining one or more nucleic acid sequences in a sample with multiple primers comprising randomized nucleotide sequences, said randomized sequences being sufficiently randomized ~~to provide nonpreferential start sites for amplification of the sample nucleic acid sequences~~ such that substantially all of the nucleic acid sequences of a biological entity are represented among amplification products;

(b) ~~performing a plurality of cycles of a polymerase chain reaction to randomly amplify~~ amplifying the sample nucleic acid sequences ; to produce nucleic acid amplification products;

(c) combining the amplification products with an array of predetermined nucleic acid sequences including redundancies such that at least a portion of the amplification products hybridize to the array; and

(d) detecting amplification products that hybridize ~~hybridized~~ to the array.

Claim 17. (Currently amended) The method of Claim 16, wherein a detectable nucleoside triphosphate is incorporated to produce detectable amplification products, ~~further comprising detecting the detectable amplification products hybridized to the array.~~

Claim 18. (Currently amended) The method of Claim ~~17~~ 16, further comprising relating the detected amplification products to at least one biological entity in the sample.

*U.S. Patent Application Serial No. 10/630384
Amendment and Response to Office Action
Page 3 of 26*

Claim 19. (Previously presented) The method of Claim 16, wherein the primers are four to fifteen nucleotides in length.

Claim 20. (Previously presented) The method of Claim 16, wherein the array of predetermined nucleic acid sequences is immobilized on a surface.

Claim 21. (Previously presented) The method of Claim 17, wherein the detectable amplification products are enzymatically detected.

Claim 22. (Currently amended) The method of Claim 17 ~~16~~, wherein the detectable nucleoside triphosphate is labeled with biotin ~~biotinylated~~.

Claim 23. (Currently amended) The method of Claim 17 ~~16~~, wherein the detectable nucleoside triphosphate is fluorescently labeled.

Claim 24. (Currently amended) The method of Claim 17 ~~16~~, wherein the detectable nucleoside triphosphate is labeled with digoxigenin.

Claim 25. (Previously presented) The method of Claim 16, wherein the detectable nucleoside triphosphate is labeled with radiolabel.

Claim 26. (Previously presented) The method of Claim 20, wherein the surface is an opaque membrane.

Claim 27. (Previously presented) The method of Claim 20, wherein the surface is silica-based.

U.S. Patent Application Serial No. 10/630384
Amendment and Response to Office Action
Page 4 of 26

Claim 28. (Previously presented) The method of Claim 16, wherein the predetermined nucleic acid sequences are at predetermined positions on the array and wherein the nucleic acid sequences at two or more predetermined positions characterize a different biological entity or variant of a biological entity.

Claim 29. (Currently amended) The method of Claim 16, further comprising relating the detected amplification products to the phylogeny of at least one biological entity wherein the sample comprises multiple biological entities.

Claim 30. (Currently amended) The method of Claim 16, wherein the biological entity comprises is a pathogen.

Claim 31. (Previously presented) The method of Claim 16, wherein the predetermined nucleic acid sequences are more than 30 nucleotides in length.

Claim 32. (Currently amended) A method for detecting one or more biological entities in a sample, comprising:

(a) combining one or more nucleic acid sequences in a sample with multiple primers comprising randomized nucleotide sequences, said randomized sequences being sufficiently randomized ~~to provide amplification products having nucleotide sequences of nonpreferential length~~ such that substantially all of the nucleic acid sequences of a biological entity are represented among amplification products;

(b) ~~performing a plurality of cycles of a polymerase chain reaction to~~ randomly ~~amplify~~ amplifying the sample nucleic acid sequences to produce nucleic acid amplification products; and,

(c) combining the amplification products with an array of predetermined nucleic acid sequences including positive controls, negative controls and redundancies such that at least a portion of the amplification products hybridize to the array; and

U.S. Patent Application Serial No. 10/630384
Amendment and Response to Office Action
Page 5 of 26

(d) detecting amplification products that hybridize ~~hybridized~~ to the array.

Claim 33. (Currently amended) The method of Claim 32, wherein a detectable nucleoside triphosphate is incorporated to produce detectable amplification products, ~~further comprising detecting the detectable amplification products hybridized to the array.~~

Claim 34. (Currently amended) The method of Claim ~~32~~ 33, further comprising relating the detected amplification products to at least one biological entity in the sample.

Claim 35. (Previously presented) The method of Claim 32, wherein the primers are four to fifteen nucleotides in length.

Claim 36. (Previously presented) The method of Claim 32, wherein the array of predetermined nucleic acid sequences is immobilized on a surface.

Claim 37. (Previously presented) The method of Claim 33, wherein the detectable amplification products are enzymatically detected.

Claim 38. (Currently amended) The method of Claim ~~33~~ 32, wherein the detectable nucleoside triphosphate is labeled with biotin ~~biotinylated~~.

Claim 39. (Currently amended) The method of Claim ~~33~~ 32, wherein the detectable nucleoside triphosphate is fluorescently labeled.

Claim 40. (Currently amended) The method of Claim ~~33~~ 32, wherein the detectable nucleoside triphosphate is labeled with digoxigenin.

*U.S. Patent Application Serial No. 10/630384
Amendment and Response to Office Action
Page 6 of 26*

Claim 41. (Previously presented) The method of Claim 32, wherein the detectable nucleoside triphosphate is labeled with radiolabel.

Claim 42. (Previously presented) The method of Claim 36, wherein the surface is an opaque membrane.

Claim 43. (Previously presented) The method of Claim 36, wherein the surface is silica-based.

Claim 44. (Previously presented) The method of Claim 32, wherein the predetermined nucleic acid sequences are at predetermined positions on the array and wherein the nucleic acid sequences at two or more predetermined positions characterize a different biological entity or variant of a biological entity.

Claim 45. (Currently amended) The method of Claim 32, ~~wherein the sample comprises multiple biological entities~~ further comprising relating the detected amplification products to the phylogeny of at least one biological entity.

Claim 46. (Currently amended) The method of Claim 32, wherein the biological entity comprises is a pathogen.

Claim 47. (Previously presented) The method of Claim 32, wherein the predetermined nucleic acid sequences are more than 30 nucleotides in length.

Claim 48. (Currently amended) A method for detecting one or more biological entities in a sample, comprising:

(a) combining nucleic acid sequences in a sample with multiple primers comprising randomized nucleotide sequences, said randomized sequences being sufficiently randomized

U.S. Patent Application Serial No. 10/630384
Amendment and Response to Office Action
Page 7 of 26

such that substantially ~~an entirety~~ all of the nucleic acid sequences of a biological entity are represented among amplification products;

(b) ~~performing a plurality of cycles of a polymerase chain reaction to randomly amplify~~ amplifying the sample nucleic acid sequences to produce nucleic acid amplification products,

(c) combining the ~~multiple~~ amplification products with an array of predetermined nucleic acids having a known spatial arrangement or relationship to each other; and

(d) detecting amplification products that hybridize ~~hybridized~~ to the array.

Claim 49. (Currently amended) The method of Claim 48 wherein a detectable nucleoside triphosphate is incorporated to produce detectable amplification products, ~~further comprising detecting the detectable amplification products that hybridized to the array.~~

Claim 50. (Currently amended) The method of Claim ~~48~~ 49, further comprising relating the detected amplification products to at least one biological entity in the sample.

Claim 51. (Previously presented) The method of Claim 48, wherein the primers are four to fifteen nucleotides in length.

Claim 52. (Previously presented) The method of Claim 48, wherein the array of predetermined nucleic acid sequences is immobilized on a surface.

Claim 53. (Previously presented) The method of Claim 49, wherein the detectable amplification products are enzymatically detected.

Claim 54. (Currently amended) The method of Claim ~~49~~ 48, wherein the detectable nucleoside triphosphate is labeled with biotin ~~biotinylated~~.

*U.S. Patent Application Serial No. 10/630384
Amendment and Response to Office Action
Page 8 of 26*

Claim 55. (Currently amended) The method of Claim 49 48, wherein the detectable nucleoside triphosphate is fluorescently labeled.

Claim 56. (Currently amended) The method of Claim 49 48, wherein the detectable nucleoside triphosphate is labeled with digoxigenin.

Claim 57. (Currently amended) The method of Claim 49 48, wherein the detectable nucleoside triphosphate is labeled with radiolabel.

Claim 58. (Previously presented) The method of Claim 52, wherein the surface is an opaque membrane.

Claim 59. (Previously presented) The method of Claim 52, wherein the surface is silica-based.

Claim 60. (Previously presented) The method of Claim 48, wherein the predetermined nucleic acids are at predetermined positions on the array and wherein the nucleic acid sequences at two or more predetermined positions characterize a different biological entity or variant of a biological entity.

Claim 61. (Currently amended) The method of Claim 48, ~~wherein the sample comprises multiple biological entities~~ further comprising relating the detected amplification products to the phylogeny of at least one biological entity.

Claim 62. (Currently amended) The method of Claim 48, wherein the biological entity is comprises a pathogen.

U.S. Patent Application Serial No. 10/630384
Amendment and Response to Office Action
Page 9 of 26

Claim 63. (Previously presented) The method of Claim 48, wherein the predetermined nucleic acid sequences are more than 30 nucleotides in length.

Claims 64-79 (canceled)

Claim 80. (Currently amended) A method for detecting one or more biological entities in a sample, comprising:

(a) combining nucleic acid sequences in a sample with multiple primers comprising randomized nucleotide sequences, said randomized sequences being sufficiently randomized to ~~provide nonpreferential start sites for amplification of the sample nucleic acid sequences~~ such that substantially ~~an entirety~~ all of the nucleic acid sequences of the biological entity are represented among amplification products;

(b) ~~performing a plurality of cycles of a polymerase chain reaction to randomly amplify~~ amplifying the sample nucleic acid sequences at each cycle of the polymerase chain reaction, to produce nucleic acid amplification products; and,

(c) combining the ~~multiple~~ amplification products with an array of predetermined nucleic acids including redundancies such that at least a portion of the amplification products hybridize to the array, wherein the redundancies on the array comprise more than one copy of the same nucleic acid sequence; and

(d) detecting amplification products that hybridize ~~hybridized~~ to the array.

Claim 81. (Currently amended) The method of Claim 80 wherein a detectable nucleoside triphosphate is incorporated, ~~further comprising detecting the detectable amplification products that hybridized to the array.~~

Claim 82. (Previously presented) The method of Claim 81, further comprising relating the detected amplification products to at least one biological entity in the sample.

*U.S. Patent Application Serial No. 10/630384
Amendment and Response to Office Action
Page 10 of 26*

Claim 83. (Previously presented) The method of Claim 80, wherein the primers are four to fifteen nucleotides in length.

Claim 84. (Previously presented) The method of Claim 80, wherein the array of predetermined nucleic acid sequences is immobilized on a surface.

Claim 85. (Previously presented) The method of Claim 81, wherein the detectable amplification products are enzymatically detected.

Claim 86. (Currently amended) The method of Claim 81 ~~80~~, wherein the detectable nucleoside triphosphate is labeled with biotin ~~biotinylated~~.

Claim 87. (Currently amended) The method of Claim 81 ~~80~~, wherein the detectable nucleoside triphosphate is fluorescently labeled.

Claim 88. (Currently amended) The method of Claim 81 ~~80~~, wherein the detectable nucleoside triphosphate is labeled with digoxigenin.

Claim 89. (Previously presented) The method of Claim 80, wherein the detectable nucleoside triphosphate is labeled with radiolabel.

Claim 90. (Previously presented) The method of Claim 84, wherein the surface is an opaque membrane.

Claim 91. (Previously presented) The method of Claim 84, wherein the surface is silica-based.

U.S. Patent Application Serial No. 10/630384
Amendment and Response to Office Action
Page 11 of 26

Claim 92. (Previously presented) The method of Claim 80, wherein the predetermined nucleic acids are at predetermined positions on the array and wherein the nucleic acid sequences at two or more predetermined positions characterize a different biological entity or variant of a biological entity.

Claim 93. (Currently amended) The method of Claim 80, ~~wherein the sample comprises multiple biological entities~~ further comprising relating the detected amplification products to the phylogeny of at least one biological entity.

Claim 94. (Currently amended) The method of Claim 80, wherein the biological entity is comprises a pathogen.

Claim 95. (Previously presented) The method of Claim 80, wherein the predetermined nucleic acid sequences are more than 30 nucleotides in length.

Claim 96. (Previously presented) A method for detecting one or more biological entities of a plurality of preselected biological entities potentially present in a sample, comprising:

(a) combining nucleic acid sequences in the sample with multiple primers comprising randomized nucleotide sequences, the randomized sequences being sufficiently randomized to ~~provide nonpreferential start sites for amplification of the sample nucleic acid sequences~~ such that substantially all of the nucleic acid sequences of a biological entity are represented among amplification products;

(b) ~~performing a plurality of cycles of a polymerase chain reaction to randomly amplify~~ amplifying the sample nucleic acid sequences to produce amplification products; and,

(c) hybridizing the amplification products to an array of predetermined nucleic acid sequences at predetermined positions on the array in a predetermined pattern, wherein the nucleic acid sequences at the predetermined positions characterize at least one of the plurality of preselected biological entities; and

U.S. Patent Application Serial No. 10/630384
Amendment and Response to Office Action
Page 12 of 26

(d) detecting amplification products that hybridize to the array.

Claim 97. (Previously presented) The method of Claim 96, wherein a detectable nucleoside triphosphate is incorporated to produce detectable multiple amplification products.

Claim 98. (Previously presented) The method of Claim 96, wherein the method simultaneously detects two or more biological entities.

Claim 99. (Previously presented) The method of Claim 96, wherein the plurality of preselected biological entities is greater than twenty-five.

Claim 100. (Previously presented) The method of Claim 96, wherein the plurality of preselected biological entities is greater than fifty.

Claim 101. (Previously presented) The method of Claim 96, wherein the plurality of preselected biological entities is greater than one hundred.

Claim 102. (Previously presented) The method of Claim 96, wherein the plurality of preselected biological entities is greater than one thousand.

Claim 103. (Previously presented) The method of Claim 96, wherein the nucleic acid sequences at the predetermined positions comprise a continuum of highly conserved to highly specific nucleic acids.

Claim 104. (Currently amended) The method of Claim 96, wherein the method provides information about the biological entity ~~even if identification of the biological entity cannot be ascertained.~~

U.S. Patent Application Serial No. 10/630384
Amendment and Response to Office Action
Page 13 of 26

Claim 105. (Previously presented) The method of Claim 96, wherein the method provides information on the biological entity including one or more of the following: the kingdom, phylum, class, order, family, genus and species of the biological entity.

Claim 106. (Previously presented) The method of Claim 96, wherein the method provides the ability to extract information resident in a genome of the biological entity.

Claim 107. (Currently amended) The method of Claim 96, wherein the method provides the ability to extract information about drug ~~antibiotic~~ resistance of the biological entity.

Claim 108. (Currently amended) The method of Claim 96, wherein the method provides the ability to extract information about the identity of a pathogen present in ~~virulence~~ of the biological entity.

Claim 109. (Currently amended) The method of Claim 96, wherein the method provides the ability to extract information about a pathogen comprising a communicable disease ~~transmissibility of the biological entity~~.

Claim 110. (Previously presented) The method of Claim 96, wherein the method provides the ability to extract information about treatment modalities for the biological entity.

Claim 111. (Previously presented) The method of Claim 96, wherein the method detects a genetic alteration in the biological entity.

Claim 112. (Previously presented) The method of Claim 96, wherein the method detects an induced genetic alteration in the biological entity.

*U.S. Patent Application Serial No. 10/630384
Amendment and Response to Office Action
Page 14 of 26*

Claim 113. (Previously presented) The method of Claim 96, wherein one or more of the predetermined nucleic acid sequences are redundant on the array.

Claim 114. (Previously presented) The method of Claim 96, wherein two or more of the predetermined nucleic acid sequences are overlapping sequences.

Claim 115. (Previously presented) The method of Claim 96, wherein two or more of the predetermined nucleic acid sequences are overlapping sequences of a single biological entity.

Claim 116. (Previously presented) The method of Claim 96, wherein two or more of the predetermined nucleic acid sequences are sub-sequences of each other.

Claim 117. (Previously presented) The method of Claim 96, wherein two or more of the predetermined nucleic acid sequences are nested subset sequences of each other.

Claim 118. (Previously presented) The method of Claim 96, wherein the detectable amplification products are hybridized to the array under high stringency conditions.

Claim 119. (Previously presented) The method of Claim 96, wherein the detectable amplification products are hybridized to the array under low stringency conditions.

Claim 120. (Previously presented) The method of Claim 96, wherein the detectable amplification products are hybridized to the array under hybridization conditions between about 50 and 65 degrees Celsius.

Claim 121. (Previously presented) The method of Claim 96, wherein the primers are four to fifteen nucleotides in length.

U.S. Patent Application Serial No. 10/630384
Amendment and Response to Office Action
Page 15 of 26

Claim 122. (Previously presented) The method of Claim 96, wherein the primers are four to nine nucleotides in length.

Claim 123. (Previously presented) The method of Claim 96, wherein the primers are four to six nucleotides in length.

Claim 124. (Previously presented) The method of Claim 96, wherein the primers are greater than six nucleotides in length.

Claim 125. (Currently amended) A method for obtaining information resident in a genetic code of one or more biological entities in a sample, comprising:

(a) combining nucleic acid sequences in the sample with multiple primers comprising randomized nucleotide sequences, the randomized sequences being sufficiently randomized to ~~provide nonpreferential start sites for amplification of the sample nucleic acid sequences~~ such that substantially all of the nucleic acid sequences of a biological entity are represented among amplification products;

(b) ~~performing a plurality of cycles of a polymerase chain reaction to randomly amplify~~ amplifying the sample nucleic acid sequences to produce amplification products;

(c) hybridizing the amplification products to an array of predetermined nucleic acid sequences at predetermined positions on the array in a predetermined pattern; and ,

(d) detecting ~~hybridized~~ the amplification products that hybridize to ~~on~~ the array to obtain genetic information about at least one biological entity in the sample ~~the biological entity.~~

Claim 126. (canceled)

Claim 127. (Previously presented) The method of Claim 125, wherein the genetic information characterizes the biological entity.

*U.S. Patent Application Serial No. 10/630384
Amendment and Response to Office Action
Page 16 of 26*

Claim 128. (Previously presented) The method of Claim 125, wherein the genetic information identifies the biological entity.

Claim 129. (Previously presented) The method of Claim 125 wherein the genetic information monitors the biological entity.

Claim 130. (Previously presented) The method of Claim 125, wherein the genetic information monitors the presence of the biological entity.

Claim 131-135 (canceled)

Claim 136. (Previously presented) The method of Claim 17, wherein the detectable nucleoside triphosphate is incorporated during amplification.

Claim 137. (Previously presented) The method of Claim 33, wherein the detectable nucleoside triphosphate is incorporated during amplification.

Claim 138. (Previously presented) The method of Claim 49, wherein the detectable nucleoside triphosphate is incorporated during amplification.

Claim 139. (Previously presented) The method of Claim 81, wherein the detectable nucleoside triphosphate is incorporated during amplification.

Claim 140. (Previously presented) The method of Claim 97, wherein the detectable nucleoside triphosphate is incorporated during amplification.

U.S. Patent Application Serial No. 10/630384
Amendment and Response to Office Action
Page 17 of 26

Claim 141. (Currently amended) A method for detecting one or more pathogens in a sample, wherein the pathogens are used for the production of biological weapons for terrorism or battlefield use, comprising:

(a) combining one or more nucleic acid sequences in a sample with multiple primers comprising randomized nucleotide sequences, said randomized sequences being sufficiently randomized ~~to provide nonpreferential start sites for amplification of the sample nucleic acid sequences~~ such that substantially all of the nucleic acid sequences of a biological entity are represented among amplification products;

(b) ~~performing a plurality of cycles of a polymerase chain reaction to randomly amplify~~ amplifying the sample nucleic acid sequences, to produce nucleic acid amplification products,

(c) combining the amplification products with an array of predetermined nucleic acid sequences including redundancies such that at least a portion of the amplification products hybridize to the array; and

(d) detecting amplification products that hybridize ~~hybridized~~ to the array.

Claim 142. (Previously presented) The method of Claim 141, wherein the biological pathogen comprises *Bacillus anthracis* or *Yersinia pestis*.

Claim 143. (New) The method of Claim 16 wherein the redundancies on the array comprise more than one distinct nucleic acid sequence from a predetermined organism.

Claim 144. (New) The method of Claim 16 wherein the array provides broad identification, specific identification, or both broad and specific identification of the one or more biological entities detected.

Claim 145. (New) The method of Claim 16, wherein the primers are four to nine nucleotides in length.

*U.S. Patent Application Serial No. 10/630384
Amendment and Response to Office Action
Page 18 of 26*

Claim 146. (New) The method of Claim 16, wherein the primers are four to six nucleotides in length.

Claim 147. (New) The method of Claim 16, wherein the nucleic acid amplification products are produced by performing a plurality of cycles of a polymerase chain reaction to randomly amplify the sample nucleic acid sequences.